Identification of a microRNA that activates gene expression by repressing nonsense-mediated RNA decay.

Journal: Mol Cell

Publication Year: 2011

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PubMed link: 21596314

Funding Grants: Interdisciplinary Stem Cell Training Program at UCSD II

Public Summary:
Nonsense-mediated decay (NMD) degrades both normal and aberrant transcripts harboring stop codons in particular contexts. Mutations that perturb NMD cause neurological disorders in humans, suggesting that NMD has roles in the brain. Here, we identify a brain-specific microRNA-miR-128-that represses NMD and thereby controls batteries of transcripts in neural cells. miR-128 represses NMD by targeting the RNA helicase UPF1 and the exon-junction complex core component MLN51. The ability of miR-128 to regulate NMD is a conserved response occurring in frogs, chickens, and mammals. miR-128 levels are dramatically increased in differentiating neuronal cells and during brain development, leading to repressed NMD and upregulation of mRNAs normally targeted for decay by NMD; overrepresented are those encoding proteins controlling neuron development and function. Together, these results suggest the existence of a conserved RNA circuit linking the microRNA and NMD pathways that induces cell type-specific transcripts during development.

Scientific Abstract:
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